



ANGES-9 (0003734-0059)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner : Scott Long

Group Art Unit : 1633

Applicants : Ryuichi Morishita et al.

Application No. : 10/564,269

Confirmation No. : 7392

Filed : February 22, 2006

For : MEDICAL COMPOSITION CONTAINING NF-KB DECOY
FOR TREATING AND PREVENTING RESPIRATORY
DISEASES AND METHOD OF USING THE SAME

New York, New York
October 25, 2007

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §§ 1.56 and 1.97, applicants hereby make of record the following documents. Pursuant to 37 C.F.R. § 1.98(a)(2) no copies of the U.S. Patent documents are provided. Copies of the Foreign Documents and Non-Patent Documents are submitted herewith .

For the Examiner's convenience, applicant has also enclosed a completed Form PTO/SB/08A, listing these documents.

UNITED STATES PATENT DOCUMENT

5,631,237	Dzau et al.	May 20, 1997
6,303,582	Eljamal et al.	October 16, 2001

FOREIGN PATENT DOCUMENT

WO 01/57204	PCT	August 9, 2001
WO 03/105780	PCT	December 24, 2003

NON-PATENT REFERENCES

Abe et al., "Specific inhibition of influenza virus RNA polymerase and nucleoprotein gene expression by circular dumbbell RNA/DNA chimeric oligonucleotides containing antisense phosphodiester oligonucleotides," *FEBS Letters*, 425(1):91-96 (1998).

Altschul et al., "Basic local alignment search tool," *Journal of Molecular Biology*, 215:403-410 (1990).

Aoki et al., "Effects of cerebroplegic solutions during hypothermic circulatory arrest and short-term recovery," *Journal of Thoracic and Cardiovascular Surgery*, 108:291-301 (1994).

Ardailou et al., "Production et activite proinflammatoire de necrose tumorale alpha dans le glomerule," *L'Academie Nationale de Medecine*, 179:103-116 (1995).

Attiga et al., "Inhibitors of prostaglandin synthesis inhibit human prostate tumor cell invasiveness and reduce the release of matrix metalloproteinases," *Cancer Research*, 60:4629-4637 (2000).

Baeuerle et al., "Function and activation of NF- κ B in the immune system," *Annual Review of Immunology*, 12:141-179 (1994).

Baker et al., "Matrix metalloproteinases, their tissue inhibitors and colorectal cancer staging," *British Journal of Surgery*, 87: 1215-1221 (2000).

Bellinger et al., "Developmental and neurologic status of children after heart surgery with hypothermic circulatory arrest or low-flow cardiopulmonary bypass," *New England Journal of Medicine*, 332:549-555 (1995).

Bennett et al., "Inhibition of vascular smooth muscle cell proliferation in vitro and in vivo by C-myc antisense oligodeoxynucleotides," *Journal of Clinical Investigation*, 93:820-828 (1994).

Berkowitz et al., "Multiple sequence elements of a single functional class are required for cyclic AMP responsiveness of the mouse c-fos promoter," *Molecular and Cellular Biology*, 9(10):4272-4281 (1989).

Bielinska et al., "Regulation of gene expression with double-stranded phosphorothioate oligonucleotides," *Science*, 250(4983):997-1000 (1990).

Bond et al., "Synergistic upregulation of metalloproteinase-9 by growth factors and inflammatory cytokines: an absolute requirement for transcription factor NF- κ B," *FEBS Letter*, 435:29-34 (1998).

Bond et al., "Nuclear factor κ B activity is essential for matrix metalloproteinase-1 and -3 upregulation in rabbit dermal fibroblasts," *Biochemical and Biophysical Research Communications*, 264:561-567 (1999).

Briata et al., "c-myc Gene expression in human cells is controlled by glucose," *Biochemical and Biophysical Research Communications*, 165(3):1123-1129 (1989).

Brown et al., "Effect of phosphorothioate modification of oligodeoxynucleotides on specific protein binding," *The Journal of Biological Chemistry*, 269(43):26801-26805 (1994).

Brunner et al., "Single bilayer vesicles prepared without sonication physico-chemical properties," *Biochimica et Biophysica Acta Biomembranes*, 455(2):322-331 (1976).

Burgess et al., "The antiproliferative activity of c-myb and c-myc antisense oligonucleotides in smooth muscle cells is caused by a nonantisense mechanism," *PNAS*, 92:4051-4055 (1995).

Cereghini et al., "A liver-specific factor essential for albumin transcription differs between differentiated and dedifferentiated rat hepatoma cells," *Genes and Development*, 2(8):957-974 (1988).

Cheng et al., "Caspase inhibitor affords neuroprotection with delayed administration in a rat model of neonatal hypoxic-ischemic brain injury," *Journal of Clinical Investigation*, 101:1992-1999 (1998).

Christman et al., "Nuclear factor κ B: a pivotal role in the systemic inflammatory response syndrome and new target for therapy," *Intensive Care Medicine* 24:1131-1138 (1998).

Clemens et al., "Global cerebral ischemia activates nuclear factor- κ B prior to evidence of DNA fragmentation," *Molecular Brain Research*, 48:187-196 (1997).

Clowes et al., "Mechanisms of stenosis after arterial injury," *Laboratory Investigation*, 49(2):208-215 (1983).

Cole et al., "Efficient priming of CD8⁺ memory T cells specific for a subdominant epitope following Sendai virus infection," *Journal of Immunology*, 158:4301-4309 (1997).

Cooper et al., "Myocardial nuclear factor- κ B activity and nitric oxide production in rejecting cardiac allografts," *Transplantation*, 66(7):838-844 (1998).

Corpet, "Multiple sequence alignment with hierarchical clustering," *Nucleic Acids Research*, 16(22):10881-10890 (1988).

Coward et al., "NF- κ B and TNF- α : A Positive Autocrine Loop in Human Lung Mast Cells?," *J. Immunology*, 169:5287-5293 (2002).

Currier et al., "Restenosis after percutaneous transluminal coronary angioplasty: have we been aiming at the wrong target?," *The American College of Cardiology*, 25(2):516-520 (1995).

Davis, "The mitogen-activated protein kinase signal transduction pathway," *The Journal of Biological Chemistry*, 268(20):14553-14556 (1993).

Deamer, "Preparation and properties of ether-injection liposomes," *Annals of the New York Academy of Sciences*, 308:250-258 (1978).

Denhardt, "Oncogene-initiated aberrant signaling engenders the metastatic phenotype: synergistic transcription factor interactions are targets for cancer therapy," *Critical Reviews in Oncogenesis*, 7(3&4):261-269 (1996).

Depre et al., "Unloaded heart *in vivo* replicates fetal gene expression of cardiac hypertrophy," *Nature Medicine*, 4(11):1269-1275 (1998).

Di Paolo et al., "High glucose concentration induces the overexpression of transforming growth factor- β through the activation of a platelet-derived growth factor loop in human mesangial cells," *American Journal of Pathology*, 149(6):2095-2106 (1996).

Dzau et al., "Fusigenic viral liposome for gene therapy in cardiovascular diseases," *PNAS*, 93:11421-11425 (1996).

Eberhardt et al., "Implication of IL-1 β -induced matrix metalloproteinase-9 expression by superoxide in rat glomerular mesangial cells is mediated by increased activities of NF- κ B and activating protein-1 and involves activation of the mitogen-activated protein kinase pathways," *Journal of Immunology*, 165:5788-5797 (2000).

Farias et al., "Plasma metalloproteinase activity is enhanced in the euglobulin fraction of breast and lung cancer patients," *International Journal of Cancer*, 89:389-394 (2000).

Gaetani et al., "Metalloproteases and intracranial vascular lesions," *Neurological Research*, 21:385-390 (1999).

Gao et al., "Phosphorothioate oligonucleotides are inhibitors of human DNA polymerases and Rnase H: implications for antisense technology," *Molecular Pharmacology*, 41(1):223-229 (1992).

Gish et al., "Identification of protein coding regions by database similarity search," *Nature Genetics*, 3:266-272 (1993).

Grilli et al., "Neuroprotection by aspirin and sodium salicylate through blockade of NF- κ B activation," *Science*, 274:1383-1385 (1996).

Hagihara et al., "Widespread gene transfection into the central nervous system of primates," *Gene Therapy*, 7:759-763 (2000).

Hasan et al., "Creation of an infectious recombinant Sendai virus expressing the firefly luciferase gene from the 3' proximal first locus," *Journal of General Virology*, 78:2813-2820 (1997).

Hessel et al., "Bronchoconstriction and airway hyperresponsiveness after ovalbumin inhalation in sensitized mice," *European Journal of Pharmacology, Environmental Toxicology and Pharmacology Section 293*, 401-412 (1995)

Higgins et al., "Clustal: a package for performing multiple sequence alignment on a microcomputer," *Gene*, 73(1):237-244 (1988).

Higgins et al., "Fast and sensitive multiple sequence alignments on a microcomputer," *Computer Applications in the Biosciences*, 5(2):151-153 (1989).

Higgins et al., "Using CLUSTAL for multiple sequence alignments," *Methods in Enzymology*, 266:383-402 (1996).

Horikawa et al., "Association of latent membrane protein 1 and matrix metalloproteinase 9 with metastasis in nasopharyngeal carcinoma," *Cancer*, 89:715-723 (2000).

Howard et al., "NF- κ B is activated and ICAM-1 gene expression is upregulated during reoxygenation of human brain endothelial cells," *Neuroscience Letters*, 248:199-203 (1998).

Hu et al., "Activation of mitogen-activated protein kinases (ERK/JNK) and AP-1 transcription factor in rat carotid arteries after balloon injury," *Arteriosclerosis, Thrombosis, and Vascular Biology*, 17(11):2808-2816 (1997).

Huang et al., "Parallelization of a local similarity algorithm," *Computer Applications in the Biosciences*, 8(2):155-165 (1992).

Inaba et al., "Enhanced expression of platelet-derived growth factor- β receptor by high glucose," *Diabetes*, 45:507-512 (1996).

Ikeda et al., "Inhibition of gelatinolytic activity in tumor tissues by synthetic matrix metalloproteinase inhibitor: application of film *in situ* zymography," *Clinical Cancer Research*, 6:3290-3296 (2000).

Izumi et al., "Gene transfer of dominant-negative mutants of extracellular signal-regulated kinase and c-Jun NH2-terminal kinase prevents neointimal formation in balloon-injured rat artery," *Circulation Research*, 88:1120-1126 (2001).

Jia et al., "Suppression of human microvascular endothelial cell invasion and morphogenesis with synthetic matrixin inhibitors," *Angiogenesis: From the Molecular to Integrative Pharmacology*, Edited by Maragoudakis, Kluwer Academic/Plenum Publishers, New York (2000).

Johnston, "The characteristics required for a Sendai virus preparation to induce high levels of interferon in human lymphoblastoid cells," *Journal of General Virology*, 56:175-184 (1981).

Jonas, "Hypothermia, circulatory arrest, and the pediatric brain," *Journal of Cardiothoracic and Vascular Anesthesia*, 10:66-74 (1996).

Kaneda et al., "Gene therapy using HVJ-liposomes: the best of both worlds?," *Molecular Medicine Today*, 5:298-303 (1999).

Kanda et al., "The role of the activated form of matrix metalloproteinase-2 in urothelial cancer," *BJU International*, 86:553-557 (2000).

Karin, "The regulation of AP-1 activity by mitogen-activated protein kinases," *The Journal of Biological Chemistry*, 270(28):16483-16486 (1995).

Kawauchi et al., "Gene therapy for attenuating cardiac allograft arteriopathy using ex vivo E2F decoy transfection by HVJ-AVE-liposome method in mice and nonhuman primates," *Circulation Research*, 87(11):1063-1068 (2000).

Khaled et al., "Use of Phosphorothioate-modified oligodeoxynucleotides to inhibit NF- κ B expression and lymphocyte function," *Clinical Immunology and Immunopathology*, 86(2):170-179 (1998).

Khaled et al., "Multiple mechanisms may contribute to the cellular anti-adhesive effects of phosphorothioate oligodeoxynucleotides," *Nucleic Acids Research*, 24(4):737-745 (1996).

Kim et al., "Lipopolysaccharide activates matrix metalloproteinase-2 in endothelial cells through an NF- κ B-dependent pathway," *Biochemical and Biophysical Research Communications*, 269:401-405 (2000).

Kirino, "Delayed neuronal death in the gerbil hippocampus following ischemia," *Brain Research*, 239:57-69 (1982).

Kirklin et al., "The damaging effects of total circulatory arrest during hypothermia," *Cardiac Surgery*, 1:66-73 (1993).

Koyama et al., "Cell replication in the arterial wall: activation of signaling pathway following in vivo injury," *Circulation Research*, 82:713-721 (1998).

Kuner et al., " β -amyloid binds to p75^{NTR} and activates NF κ B in human neuroblastoma cells," *Journal of Neuroscience Research*, 54:798-804 (1998).

Kuroya et al., "Newborn virus pneumonitis (type Sendai) II Report: the isolation of a new virus possessing hemagglutinin activity," *Yokohama Medicine Bulletin*, 4(4):217-233 (1953).

Kurth et al., "Regional patterns of neuronal death after deep hypothermic circulatory arrest in newborn pigs," *Journal of Thoracic Cardiovascular Surgery*, 118:1068-1077 (1999).

La Rosa et al., "Differential regulation of the c-myc oncogene promoter by the NF- κ B rel family of transcription factors," *Molecular and Cellular Biology*, 14(2):1039-1044 (1994).

Larrouy et al., "Rnase H-mediated inhibition of translation by antisense oligodeoxyribonucleotides: use of backbone modification to improve specificity," *Gene*, 121:189-194 (1992).

Ledley, "Nonviral Gene Therapy: The Promise of Genes as Pharmaceutical Products," *Human Gene Therapy* 6:1129-1144 (1995).

Lenardo et al., "NF- κ B: A pleiotropic mediator of inducible and tissue-specific gene control," *Cell*, 58:227-229 (1989).

Libermann et al., "Activation of interleukin-6 gene expression through NF- κ B transcription factor," *Molecular and Cellular Biology*, 10(5):2327-2334 (1990).

Lim et al., "Sequence-independent inhibition of RNA transcription by DNA dumbbells and other decoys," *Nucleic Acids Research*, 25(3):575-581 (1997).

Lin et al., "Cancer chemoprevention by tea polyphenols through mitotic signal transduction blockade," *Biochemical Pharmacology*, 58:911-915 (1999).

Lindner et al., "Role of basic fibroblast growth factor in vascular lesion formation," *Circulation Research*, 68:106-113 (1991).

Liu et al., "Restenosis after coronary angioplasty," *Circulation*, 79:1374-1387 (1989).

Mann et al., "Ex-vivo gene therapy of human vascular bypass grafts with E2F decoy: the PREVENT single-centre, randomised, controlled trial," *Lancet*, 354:1493-1498 (1999).

Marcus-Sekura et al., "Techniques for using antisense oligodeoxyribonucleotides to study gene expression," *Analytical Biochemistry*, 172:289-295 (1988).

Marti, "New strategy to treat glomerular inflammation by inhibition of mesangial cell matrix metalloproteinases," Abteilung Nephrologie/Hypertonie, Inselspital, Berne, *Schweiz Med Wochenschr*, 130(21):784-8.

Miagkov et al., "NF- κ B activation provides the potential link between inflammation and hyperplasia in the arthritic joint," *PNAS*, 95:13859-13864 (1998).

- Miano et al., "Smooth muscle cell immediate-early gene and growth factor activation follows vascular injury," *Arteriosclerosis and Thrombosis*, 13(2):211-219 (1993).
- Moon et al., "Potent growth inhibition of leukemic cells by novel ribbon-type antisense oligonucleotides to c-myl,," *The Journal of Biological Chemistry*, 275(7):4647-4653 (2000).
- Morishita et al., "Single intraluminal delivery of antisense cdc2 kinase and proliferating-cell nuclear antigen oligonucleotides results in chronic inhibition of neointimal hyperplasia," *PNAS*, 90:8474-88478 (1993).
- Morishita et al., "Intimal hyperplasia after vascular injury is inhibited by antisense cdk 2 kinase oligonucleotides," *The Journal of Clinical Investigation*, 93:1458-1464 (1994).
- Morishita et al., "Novel strategy of gene therapy in cardiovascular disease with HVJ-liposome method," *Koide H. Ichikawa I (eds): Progression of Chronic Renal Diseases*, Contrib Nephrol. Basel, Karger, 118:254-264 (1996).
- Morishita et al., "In vivo transfection of cis element "decoy" against nuclear factor- κ B binding site prevents myocardial infarction," *Nature Medicine*, 3(8):894-899 (1997).
- Morishita et al., "A gene therapy strategy using a transcription factor decoy of the E2F binding site inhibits smooth muscle proliferation in vivo," *PNAS*, 92(13):5855-59 (1995).
- Mosser et al., "Use of dicistronic expression cassette encoding the green fluorescent protein for the screening and selection of cells expressing inducible gene products," *BioTechniques*, 22:150-161 (1997).
- Motokuni et al., *Nippon Rinsho*, 59(1):43-52 (2002) (Japanese Version).
- Mulligan, "The basic science of gene therapy," *Science*, 260:926-932 (1993).
- Myers et al., "Optimal alignments in linear space," *Computer Applications in the Biosciences*, 4(1):11-17 (1988).
- Natarajan et al., "Angiotensin II signaling in vascular smooth muscle cells under high glucose conditions," *Hypertension*, 33:378-384 (1999).
- Needleman et al., "A general method applicable to the search for similarities in the amino acid sequence of two proteins," *Journal of Molecular Biology*, 48:443-453 (1970).
- Neish et al., "Functional analysis of the human vascular cell adhesion molecule 1 promoter," *Journal of Experimental Medicine*, 176:1583-1593 (1992).
- Ohashi et al., "Role of p38 mitogen-activated protein kinase in neointimal hyperplasia after vascular injury," *Arteriosclerosis and Thrombosis Vascular Biology*, 20(12):2521-2526 (2000).

Okada et al., "Correlation between the hemagglutination titer and the virus particle number of HVJ," *Biken's Journal*, 4:209-213 (1961).

Ono et al., "Decoy Administration of NF-KB into the Subarachnoid Space of Cerebral Angiopathy," *Human Gene Therapy*, 9(7):1003-1011 (1998) and Ono et al., *Human Gene Therapy*, 10:335 (1999).

Osada et al., "Expression and localization of nuclear factor-kappa B subunits in cultured human paranasal sinus mucosal cells," *Rhinology*, 41:80-86 (2003).

Pagano et al., "Cyclin A is required at two points in the human cell cycle," *The EMBO Journal*, 11(3):961-971 (1992).

Pagano et al., "Association of cdk2 kinase with the transcription factor E2F during S phase," *Science*, 255 (5048):1144-1147 (1992).

Pardee, "A restriction point for control of normal animal cell proliferation," *PNAS*, 71(4):1286-1290 (1974).

Parthasarathy et al., "Aerosol delivery of liposomal all-trans-retinoic acid to the lungs," *Cancer Chemotherapy and Pharmacology*, 43:277-283 (1999).

Pauletto et al., "Smooth-muscle-cell proliferation and differentiation in neointima formation and vascular restenosis," *Clinical Science*, 87(5):467-479 (1994).

Pearson et al., "Improved tools for biological sequence comparison," *PNAS*, 85:2444-2448 (1988).

Pearson, "Using the FASTA program to search protein and DNA sequence databases," *Methods in Molecular Biology*, 24:307-331 (1994).

Pellegrini et al., "Simultaneous measurement of soluble carcinoembryonic antigen and the tissue inhibitor of metalloproteinase TIMP1 serum levels for use as markers of pre-invasive to invasive colorectal cancer," *Cancer Immunology Immunotherapy*, 49:388-394 (2000).

Peters et al., "Functional polymorphism in the matrix metalloproteinase-9 promoter as a potential risk factor for intracranial aneurysm," *Stroke*, 30:2612-2616 (1999).

Preston et al., "Evidence for pore-like opening of the blood-brain barrier following forebrain ischemia in rats," *Brain Research*, 761:4-10 (1997).

Pyles et al., "Activation of MAP kinases in vivo follows balloon overstretch injury of porcine coronary and carotid arteries," *Circulation Research*, 81:904-910 (1997).

Rappaport et al., "Relation of seizures after cardiac surgery in early infancy to neurodevelopmental outcome," *Circulation*, 97:773-779 (1998).

Rayet et al., "Aberrant *rel/nfkb* genes and activity in human cancer," *Oncogene*, 18:6938-6947 (1999).

Reich et al., "Cardiopulmonary support and physiology," *Journal of Thoracic and Cardiovascular Surgery*, 117:156-163 (1999).

Rosenblatt et al., "Human cyclin-dependent kinase 2 is activated during the S and G₂ phases of the cell cycle and associates with cyclin A," *PNAS*, 89:2824-2828 (1992).

Ross, "The pathogenesis of atherosclerosis: a perspective for the 1990s," *Nature*, 362:801-808 (1993).

Royds et al., "Response of tumour cells to hypoxia: Role of p53 and NFκB," *Journal of Clinical Patholog, Molecular Pathology*, 51:55-61 (1998).

Sakata et al., "Expression of matrix metalloproteinases (MMP-2, MMP-9, MT1-MMP) and their inhibitors (TIMP-1, TIMP-2) in common epithelial tumors of the ovary," *International Journal of Oncology*, 17:673-681 (2000).

Satriano et al., "Activation and attenuation of transcription factor NF-κB in mouse glomerular mesangial cells in response to tumor necrosis factor-α, immunoglobulin G, and adenosine 3':5'-cyclic monophosphate," *Journal of Clinical Investigation*, 94:1629-1636 (1994).

Sawa et al., "A novel strategy for myocardial protection using in vivo transfection of cis element 'decoy' against NFκB binding site," *Circulation*, 96(9):II-280-II-285 (1997).

Schneider et al., "NF-κB is activated and promotes cell death in focal cerebral ischemia," *Nature Medicine*, 5(4):554-559 (1999).

Schöler et al., "Specific interaction between enhancer-containing molecules and cellular components," *Cell*, 36(2):403-411 (1984).

Schreck et al., "Reactive oxygen intermediates as apparently widely used messengers in the activation of the NF-κB transcription factor and HIV-1," *The EMBO Journal*, 10(8):2247-2258 (1991).

Schulze-Osthoff et al., "Regulation of NF-κB activation by MAP kinase cascades," *Immunobiology*, 198:35-49 (1997).

Schwartz et al., "The intima," *Circulation Research*, 77:445-465 (1995).

Seger et al., "The MAPK signaling cascade," *The FASEB Journal*, 9(9):726-735 (1995).

Shin et al., "Effects of tumor necrosis factor-α and interferon-γ on expression of matrix metalloproteinase-2 and -9 in human bladder cancer cells," *Cancer Letters*, 159:127-134 (2000).

Simons et al., "Antisense c-myb oligonucleotides inhibit intimal arterial smooth muscle cell accumulation in vivo," *Nature*, 359:67-70 (1992).

Simons et al., "Antisense Proliferation Cell Nuclear Antigen Oligonucleotides Inhibit Hyperplasia in a Rat Carotid Artery Injury Model," *Journal of Clinical Investigation*, 93:2351-2356 (1994).

Smith, "Comparison of biosequences," *Advances in Applied Mathematics*, 2(4):482-489 (1981).

Stein et al., "Oligodeoxynucleotides as inhibitors of gene expression: a review," *Cancer Research*, 48(10):2659-2668 (1988).

Stephenson et al., "Transcription factor nuclear factor-kappa-B is activated in neurons after focal cerebral ischemia," *Journal of Cerebral Blood Flow and Metabolism*, 20:592-603 (2000).

Sullenger et al., "Analysis of *trans*-acting response decoy RNA-mediated inhibition of human immunodeficiency virus type 1 transactivation," *Journal of Virology*, 65(12):6811-6816 (1991).

Suzuki et al., "Reconstituted fusion liposomes for gene transfer *in vitro* and *in vivo*," *Gene Therapy and Regulation*, 1:65-77 (2000).

Szoka et al., "Preparation of unilamellar liposomes of intermediate size (0.1-0.2 μ m) by a combination of reverse phase evaporation and extrusion through polycarbonate membranes," *Biochimica et Biophysica Acta Biomembranes*, 601(3):559-571 (1980).

Tanaka et al., "Sequence-specific interaction of α - β -anomeric double-stranded DNA with the p50 subunit of NF κ B: application to the decoy approach," *Nucleic Acids Research*, 22(15):3069-3074 (1994).

Thompson et al., "CLUSTAL W: improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position-specific gap penalties and weight matrix choice," *Nucleic Acids Research*, 22(22):4673-4680 (1994).

Tijssen (1993) *Laboratory Techniques in Biochemistry and Molecular Biology--Hybridization with Nucleic Acid Probes* part I chapter 2 "overview of principles of hybridization and the strategy of nucleic acid probe assays", Elsevier, N.Y.

Tomita et al., "Suppressed severity of collagen-induced arthritis by *in vivo* transfection of nuclear factor κ B decoy oligodeoxynucleotides as a gene therapy," *Arthritis & Rheumatism*, 42(12):2532-2542 (1999).

Tomita et al., "Transcription factor decoy for NF κ B inhibits TNF- α -induced cytokine and adhesion molecule expression *in vivo*," *Gene Therapy*, 7(15):1326-1332 (2000).

Tomita et al., "Transcription factor decoy for NF κ B inhibits cytokine and adhesion molecule expressions in synovial cells derived from rheumatoid arthritis," *Rheumatology*, 39:749-757 (2000).

Torre et al., "Partial or global rat brain ischemia: the SCOT model," *Brain Research Bulletin*, 26(3):365-372 (1991).

Trehan et al., "Marimastat inhibits elastin degradation and matrix metalloproteinase 2 activity in a model of aneurysm disease," *British Journal of Surgery*, 86:1053-1058 (1999).

Turner et al., "Role of matrix metalloproteinase 9 in pituitary tumor behavior," *Journal of Clinical Endocrinology & Metabolism*, 85(8):2931-2935 (2000).

Vanicky et al., "Alterations in MAP2 immunostainability after prolonged complete brain ischemia in the rat," *NeuroReport*, 7:161-164 (1995).

Vogt et al., "Oxidative stress and hypoxia/reoxygenation trigger CD95 (APO-1/Fas) ligand expression in microglial cells," *FEBS Letters*, 429:67-72 (1998).

Weintraub et al., "Retinoblastoma protein switches the E2F site from positive to negative element," *Nature*, 358:259-261 (1992).

Whitmarsh et al., "Transcription factor AP-1 regulation by mitogen-activated protein kinase signal transduction pathways," *Journal of Molecular Medicine*, 74(10):589-607 (1996).

Wu et al., "NF- κ B activation of p53," *Journal of Biological Chemistry*, 269(31):20067-20074 (1994).

Yasunari et al., "Mechanisms of action of troglitazone in the prevention of high glucose-induced migration and proliferation of cultured coronary smooth muscle cells," *Circulation Research*, 81:953 (1997).

Yokoseki et al., "*cis* element decoy against nuclear factor- κ B attenuates development of experimental autoimmune myocarditis in rats," *Circulation Research*, 89:899-906 (2001).

Yonemitsu et al., "Efficient gene transfer to airway epithelium using recombinant Sendai virus," *Nature Biotechnology*, 18:970-973 (2000).

Yoshima et al., "Comparative study of the carbohydrate moieties of rat and human plasma α 1-acid glycoproteins," *Journal of Biological Chemistry*, 256(16):8476-8484 (1981).

Yoshizumi et al., "Down-regulation of the cyclin a promoter by transforming growth factor- β 1 is associated with a reduction in phosphorylated activating transcription factor-1 and cyclic AMP-responsive element-binding protein," *The Journal of Biological Chemistry*, 272(35):22259-22264 (1997).

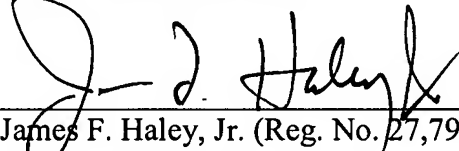
Young, BD & Anderson, MLM in *Nucleic Acid Hybridization—A Practical Approach* (eds Hames, BD & Higgins, SJ) 47–71 (IRL, Oxford, 1985).

REMARKS

Applicants further request that the cited documents be (1) fully considered by the Examiner during the course of examination of this application, and (2) printed on any patent issuing from this application. Additionally, applicants request that a copy of Form PTO/SB/08A, as considered and initialed by the Examiner, be returned with the next communication.

This Statement is submitted more than three months from the application filing date, but before the mailing of the first Office Action on the merits. In accordance with 37 C.F.R. § 1.97 (b)(3), no fee is due in connection with this Statement. However, if for any reason a fee is due, the Director is hereby authorized to charge payment of any fees required in connection with this Statement to Deposit Account No. 06-1075, Order No. 003734-0059.

Respectfully submitted,



James F. Haley, Jr. (Reg. No. 27,794)
Attorney for Applicants

ROPES & GRAY LLP
1211 Avenue of the Americas
New York, New York 10036
Tel.: (212) 596-9000
Fax.: (212) 596-9090